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Original Article

Efficacy of Adenosine for Acute Treatment of Supraventricular Tachycardia in Infants and Children

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Abstract

Background: *This study was done to assess the efficacy and adverse effects of the different doses of adenosine in the pediatric age group with respect to multiple patient variables.*

Methods: *Over a period of 1 year, 86 occasions of supraventricular tachycardia (SVT) were treated with adenosine in 81 infants and children aged between 18 days and 12 years (median of 1.3 years, SD=3). Adenosine efficacy was evaluated in terms of the patients' demographics, SVT rate, electrocardiogram characteristics, and route of drug administration.*

Results: *The dose of 50μg/kg was effective only in 24% of the SVT cases, and the additional doses of 100μg/kg, 150μg/kg, and 200μg/kg were effective in another 29% of the cases. The drug efficacy was higher in the infants than that in the older children. There were no predictors other than age for the estimation of the efficacy of the drug.*

Conclusion: *Our findings showed that the current recommended doses of adenosine are ineffective in the vast majority of children and infants with SVT. No patient-related factor other than age seems to affect the efficacy of the drug.*

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Introduction

Paroxysmal supraventricular tachycardia (SVT) is the most common symptomatic arrhythmia in young patients and affects children of all ages.[1,2] Its prevalence is estimated at more than one in 500 children.[3,4] The diagnosis of SVT is based on thorough clinical history and electrocardiogram (ECG). The characteristic features include abrupt onset and termination, fixed cycle length, normal QRS complexes, and usually an absence of clearly discernible P waves or flutter waves.[1] SVTs may be divided into many sub-types electrophysiologically; however, there are certain general principles of therapy which apply to all patients regardless of the type of SVT.[1,2] Intravenous adenosine is the first line drug for the termination of SVT in infants and children.[1,2,5-9] Most authors recommend an initial dose of 50 to 100μg/kg,[1,2,6-9] while others solely recommend an initial dose of 100μg/kg;[10] be that as it may, if such doses are ineffective, following doses by increments of 50μg/kg are recommended.

There are considerable controversies in the effectiveness and dosing of adenosine.[11-13] Patient-dependent factors such as heart rate and administration route are thought to be the predictive factors for the effectiveness of adenosine in a few studies,[14,15] while others do not find such results. The side

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effects of the drug also remain controversial.[6,16,17]

The aim of this study was to assess the effectiveness of the different doses of adenosine, as well as its side effects while considering multiple patient variables.

Methods

We conducted a prospective observational study on hospitalized children between November 2006 and 2007. During this period, 86 episodes of SVT in 81 patients (40 male and 41 female) were treated with intravenous adenosine. The diagnosis of SVT was based on clinical and ECG findings. The criteria for the rapid diagnosis of SVT were: 1- abrupt onset of arrhythmia, 2- fixed cycle length, 3- normal QRS complex duration, 4- uniform QRS complexes, 5- absence of clearly discernible P waves or flutter waves, and 6- heart rate of more than 180 per minute.

The patients were managed by pediatric cardiology fellows and trained staff in the emergency department, pediatric intensive care units, pediatric ward, and cardiac catheterization laboratory. All the patients were monitored continuously with a single-lead ECG from admission until 24 hours after the termination of the tachycardia and restoration of permanent sinus rhythm. The heart rate was recorded just before the administration of each dose of adenosine. A 12-lead ECG was obtained from all the patients after the termination of the tachycardia and was analyzed for P wave characteristics, PR interval, QRS axis and duration, presence of a delta wave, and calculation of corrected QT interval.

Adenosine was prepared as a sterile solution in 0.9% sodium chloride with 1mg/ml concentration. Each bolus was flashed immediately with physiological saline.

The route of drug administration was peripheral venous access in 48 episodes (right arm in 24, left arm in 14, right leg in 6, and left leg in 4) and central venous access in 38.

The data were analyzed with the Statistical Package for Social Sciences (SPSS, Chicago, IL) software (version 15.0) using conventional methods for mean and SDs. The comparisons between the groups were made by means of the non-parametric Mann-Whitney, Fisher, and Chi-square tests. P values of less than 0.05 were considered significant.

Results

The patients were between 18 days and 12 years of age (median=1.3, SD=3 years). Thirty-nine episodes occurred in the infants (aged 1 year or less), and the remainder in the older children. The weight of the patients ranged from 3 to 23 kg (median=8.2kg). Sixty-six patients had structural cardiac anomalies, while 38 of them had undergone palliative or corrective interventions. The types of congenital heart disease (CHD) and relative interventions are summarized in Figure 1.

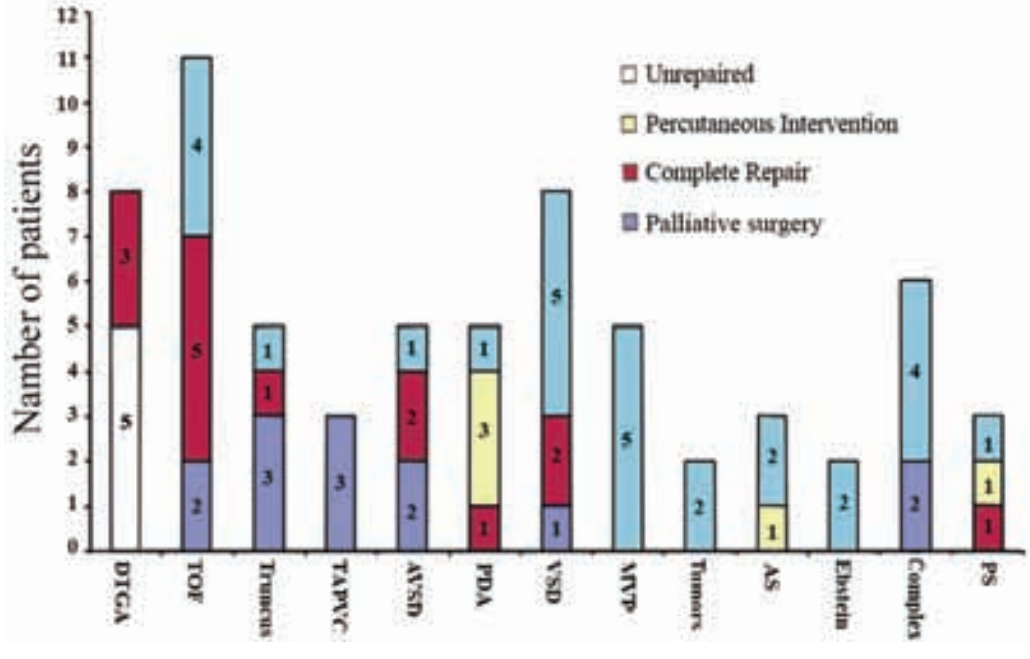

Figure 1. Types of structural heart disease and interventions in supraventricular tachycardia patients
DTGA, d- transposition of great arteries; TOF, Tetralogy of Fallot; TAPVC, Total anomalous pulmonary venous connection; AVSD, Atrioventricular septal defect; PDA, Patent ductus arteriosus; VSD, Ventricular septal defect; MVP, Mitral valve prolapse; AS, Aortic stenosis; PS, Pulmonary valve stenosis

Sixteen patients had a previous history of SVT. Fifteen patients used digoxin as a cardiac inotrope. Six patients had the Wolff-Parkinson-White (WPW) pattern on their surface ECG; two of them had a history of SVT and used propranolol. The patients' characteristics are summarized in Table 1.

Table 1. Patients' characteristics (n=81)*

Male	40 (49)
Infantile age	39 (48)
Older than 1 year	42 (52)
Structural cardiac anomaly (other than PFO and BAV)	66 (81)
Previous surgical intervention	38 (47)
History of SVT	16 (20)
Digoxin usage	15 (19)
Propranolol usage	2 (2)
Wolf- Parkinson-White Syndrome	6 (7)

*Numbers in the parentheses show the related percentages
PFO, Patent foramen ovale; BAV, Bicuspid aortic valve; SVT, Supraventricular tachycardia

The patients were divided into 2 age groups according to different reported results in previous studies.[13,15] Group I (infants group) comprised 37 patients (18 males) at the age of 1 year or less, and Group II (children group) consisted of 44 patients (22 males).

In 20 patients vagal maneuvers had been tried before adenosine administration without any success. Adenosine was given to 81 patients for 86 episodes of SVT.

The initial dose was 50μg/kg in 76 episodes and 100μg/kg in 10. The starting dose of 100μg/kg was based on personal physician judgment without any protocol or patient difference. With each dose, the cycle of arrhythmia was broken initially in many episodes but early re-initiation of arrhythmia occurred in some. In the most persistent episodes, higher doses of the drug were administered after 2-4 minutes. Many persistent episodes were treated with other drugs in the course of treatment. The effects of the different doses of adenosine and type of management in the persistent episodes are summarized in Table 2. Because of the short half-life of adenosine (less than 15 seconds), the accumulation effect was not considered.

In 35 (40.7%) episodes arrhythmia was not stopped by the current doses of adenosine; it was ineffective in 8 (20.5%) infants and 27 (57.4%) children. This difference was statistically significant ($p<0.001$). Permanent control of arrhythmia with adenosine by doses up to 200μg/kg was 69.2% in the infants compared with 40.4% in the older children ($p=0.008$).

Factors other than age (sex, history of previous SVT, presence of CHD, previous cardiac surgery, anti-arrhythmic drug use, SVT rate, ECG characteristics, and route of drug administration) were not correlated statistically with adenosine efficacy.

All the patients who did not respond to adenosine were treated with other usual anti-arrhythmic drugs successfully (18 episodes with amiodarone, 12 with verapamil, 4 with digoxin, 4 with propranolol, and 2 with procainamide). No patient needed cardioversion.

No important side effect was detected after the administration of adenosine; note that transient complete heart block was not considered as a drug adverse effect.

Discussion

Adenosine is a purine nucleoside with a half-life of 15-30 seconds in humans.[11] Its mechanism of action includes a direct effect on the activation of the adenosine-sensitive potassium current.[18] The increase in potassium conductance shortens atrial action potential duration, hyperpolarizes the membrane potential, and decreases atrial contractility.

Similar changes occur in the sinus and atrioventricular (AV) nodes. In addition to these direct effects, adenosine antagonizes catecholamine-stimulated adenylate cyclase activity.[18] When administered as a rapid intravenous bolus, adenosine should produce transient AV node block, terminating tachycardia using the AV node.[19] These effects on the AV node and sinuatrial (SA) node will be brief, allowing normal sinus rhythm to resume. Even if the AV node block fails to terminate tachycardia, the resultant alteration in the AV relationship provides important diagnostic information.

Table 2. Treatment results in 86 episodes of supraventricular tachycardia in our study*

Adenosine dose	Completely controlled episodes	Transiently controlled episodes	Uncontrolled episodes	Controlled episodes with other drugs
50μg/kg (used for 76 episodes)	18	10	48	2 (Verapamil: 2)
100μg/kg (used for 66 episodes)	8	20	38	8 (Amiodarone: 4 Verapamil: 4)
150μg/kg (used for 50 episodes)	16	13	21	22 (Amiodarone: 8 Verapamil: 6 Digoxin: 4 Propranolol: 4)
200μg/kg (used for 12 episodes)	4	4	4	8 (Amiodarone: 6 procainamide: 2)

*Adenosine was used 204 times for 86 episodes of supraventricular tachycardia (some episodes needed more than one dose of the drug). In 46 (53%) of the episodes, it was effective. All non-responding episodes to adenosine were treated with other antiarrhythmic drugs successfully.

Primary atrial tachycardia or ventricular tachycardia occasionally may be terminated by adenosine.[1] Reinitiating of tachycardia may limit the clinical efficacy of this drug. A possible mechanism is the sinus acceleration that follows a bolus dose. This is a common mechanism of the initiation of SVT in small infants.[19]

The initial recommended dose of adenosine varies between 50 to 150μg/kg. Most authors recommend an initial dose of 50 to 100μg/kg,[1,2,6-9] while others solely recommend an initial dose of 100μg/kg.[10] Overholt et al.[20] reported a mean effective dose of 114-131 μg/kg. Till et al.[6] found a median dose of 150μg/kg to be effective. Dixon et al.[12] reported that the dose of 50 μg/kg was effective in less than 10% of infants and children and that the dose of 100μg/kg was effective in less than 25% of infants and 50% of children.

Sherwood et al.[10] found a 16% response to 50μg/kg. Losek et al.[9] showed a 22% efficacy for doses up to 100μg/kg.

We found that the dose of 50μg/kg was effective in 24%, doses up to 100μg/kg in 30%, doses up to 150μg/kg in 49%, and doses up to 200μg/kg in 53% of the cases.

A few researchers have reported the effect of SVT rate[14] and route of drug administration[15] on the efficacy of the drug. We studied multiple factors, including patient demographics (age, sex), patient history (previous SVT, CHD, antiarrhythmic drug use, and previous cardiac surgery), SVT rate, basal ECG characteristics (rate and rhythms, P wave characteristics, PR interval, QRS axis and duration, presence of delta wave, and QTC), and route of drug administration. We found that none of these factors other than age influenced the efficacy of the drug.

Dixon et al.[6] found a lower response to adenosine in infants compared to children. Contrary to their findings, we found a higher response to adenosine in the infants by comparison with the children (69% vs. 40%, P=0.008).

Some researchers have demonstrated the side effects of the drug.[10,14] We found no important side effects after the administration of adenosine; it is worthy of note, however, that we did not consider transient complete heart block as a drug adverse effect.

Conclusion

Our findings showed that the current recommended adenosine doses for the acute management of SVT might be ineffective in the vast majority of cases. Chiming in with some previous studies, the present study highlights the need for a review of the dose protocol of adenosine in SVT. We would propose different dose references for infants and children in light of significant differences in drug response. Our findings confirm that nearly all SVT episodes can be controlled with routine drugs and that adenosine is a safe drug with doses up to 200 μg/kg.

We found that multiple patient variables such as sex, history of previous SVT, presence of CHD, previous cardiac surgery, anti-arrhythmic drug use, SVT rate, ECG characteristics, and route of drug administration do not affect the efficacy of adenosine.

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